NEWS RELEASE

Natera Announces Enrollment of First Patients in the HEROES Clinical Trial in Metastatic HER2+ Breast Cancer

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HEROES is Natera's first clinical trial using Signatera™ to guide de-escalation of therapy in patients with metastatic HER2+ breast cancer

Approximately 170 patients are expected to enroll in up to 35 sites in France

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and genetic testing, today announced the enrollment of the first patients in the HEROES clinical trial. HEROES is a multi-center, phase II trial that explores the discontinuation or de-escalation of anti-HER2 targeted therapy among patients with metastatic HER2+ breast cancer. The trial is supported by funding from the French Ministry of Health through the Hospital Clinical Research Program (PHRC) and is being sponsored by Unicancer. It is being developed within Unicancer's French Breast Cancer Intergroup (UCBG) network.

Human epidermal growth factor receptor 2 (HER2) is a type of protein found in cancer cells that can cause rapid cancer growth when higher than normal levels are present. Between 15%-20% of breast tumors are HER2+.[1] Current standard-of-care (SOC) recommendations for maintenance treatment include the use of anti-HER2 therapies, which for many patients means remaining on the drug for life.

The HEROES (NCT06450314) trial will enroll approximately 170 metastatic HER2+ breast cancer patients who have discontinued anti-HER2 maintenance therapy. The primary endpoint of the study is 1-year progression-free survival in the Signatera-negative cohort. It will also assess ctDNA dynamics and quality-of-life measures to gain deeper

insights into the potential for ctDNA-guided de-escalation of treatment in patients with no detectable molecular disease burden.

Highlights from the study protocol include:

- At baseline, all patients are currently being treated with SOC anti-HER2 targeted therapies and have been on therapy for two or more years.
- Signatera-negative patients at baseline will stop treatment and will be monitored with serial Signatera testing and diagnostic imaging. If at any point during the trial radiological progression is confirmed or a patient becomes Signatera-positive, prior drug therapy will resume or a new treatment will begin.
- Signatera-positive patients at baseline will continue maintenance therapy and will not move forward in the trial.

“The HEROES study could significantly reshape the way oncologists treat patients with metastatic HER2+ breast cancer,” said Thibault de la Motte Rouge, M.D., Ph.D., principal investigator of the trial and medical oncologist at the Comprehensive Cancer Centre Eugène Marquis (Rennes, France), where he currently holds the position of research director. “This could also pave the way for future research into ctDNA-guided treatment de-escalation in breast cancer.”

“We are excited to see the first patients enrolled in the HEROES clinical trial,” said Angel Rodriguez, M.D., senior medical director of oncology at Natera. “Safely discontinuing treatment has been a long-lasting dilemma in HER2 metastatic breast cancer. With Signatera monitoring, we hope oncologists can identify the patients without detectable disease who may be able to avoid additional therapy that can be costly and potentially harmful to their care.”

About Signatera

Signatera is a personalized, tumor-informed, molecular residual disease test for patients previously diagnosed with cancer. Custom-built for each individual, Signatera uses circulating tumor DNA to detect and quantify cancer left in the body, identify recurrence earlier than standard-of-care tools, and help optimize treatment decisions. The test is available for clinical and research use and is covered by Medicare for patients with colorectal cancer, breast cancer, ovarian cancer, and muscle-invasive bladder cancer, as well as for immunotherapy monitoring of any solid tumor. Signatera has been clinically validated across multiple cancer types and indications, with published evidence in over 100 peer-reviewed papers.

About Natera

Natera™ is a global leader in cell-free DNA and genetic testing, dedicated to oncology, women’s health, and organ

health. We aim to make personalized genetic testing and diagnostics part of the standard of care to protect health and inform earlier, more targeted interventions that help lead to longer, healthier lives. Natera's tests are validated by more than 250 peer-reviewed publications that demonstrate high accuracy. Natera operates ISO 13485-certified and CAP-accredited laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) in Austin, Texas, and San Carlos, California. For more information, visit **www.natera.com**.

About Unicancer

Unicancer is the only French hospital network 100% dedicated to the fight against cancer and the only national hospital federation dedicated to oncology. It brings together 18 Centres de lutte contre le cancer (CLCC), private non-profit healthcare establishments, spread over 20 hospital sites in France, as well as two affiliated member establishments. The CLCCs treat nearly 530,000 patients per year (in short stays, home hospitalisation and outpatient procedures).

Unicancer is also the leading academic promoter of clinical trials in oncology at the European level, with 106 active clinical trials promoted in 2020 and nearly 7,600 patients included. Unicancer also runs flagship programmes that use real-life data to improve knowledge and the evaluation of therapeutic strategies, particularly through the ESME platforms, which bring together data from more than 76,000 cancer patients.

Recognised as a leader in research in France, the Unicancer network enjoys a worldwide reputation with the production of one third of French publications of international scope in oncology (source: bibliometric study/Thomson Reuters). In total, nearly 700 clinical trials (inclusions or follow-ups) were promoted in 2020 by the Unicancer network, more than 14% of CLCC patients are included in clinical trials and more than half of the PHRCs are allocated to CLCCs. The 18 CLCCs and the Unicancer R&D department are ISO 9001:2015 certified for their clinical research.

Forward-Looking Statements

All statements other than statements of historical facts contained in this press release are forward-looking statements and are not a representation that Natera's plans, estimates, or expectations will be achieved. These forward-looking statements represent Natera's expectations as of the date of this press release, and Natera disclaims any obligation to update the forward-looking statements. These forward-looking statements are subject to known and unknown risks and uncertainties that may cause actual results to differ materially, including with respect to whether the results of clinical or other studies will support the use of our product offerings, the impact of results of such studies, our expectations of the reliability, accuracy, and performance of our tests, or our expectations of the benefits of our tests and product offerings to patients, providers, and payers. Additional risks and uncertainties are discussed in greater detail in "Risk Factors" in Natera's recent filings on Forms 10-K and 10-Q,

and in other filings Natera makes with the SEC from time to time. These documents are available at **www.natera.com/investors** and **www.sec.gov**.

References

1. American Cancer Society. Breast Cancer HER2 Status.**https://www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html**

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